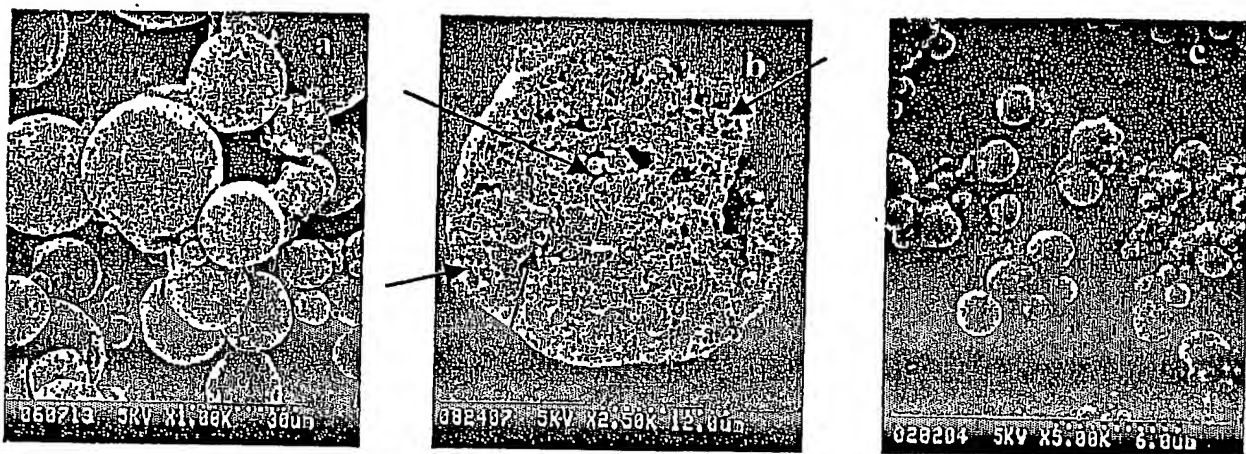


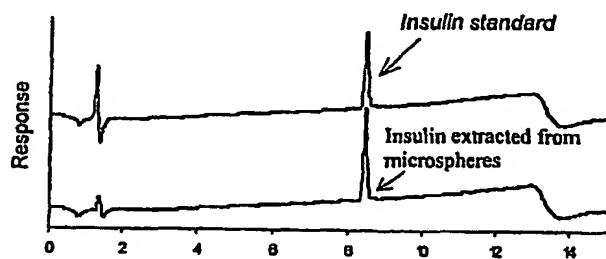
1/8

Figure 1. SEM micrographs of insulin-loaded ACHES-PLGA composite microspheres (a), interior structure of a fractured microsphere (b, arrows point to embedded ACHES microparticles) and freeze dried ACHES hydrogel microparticles (c).



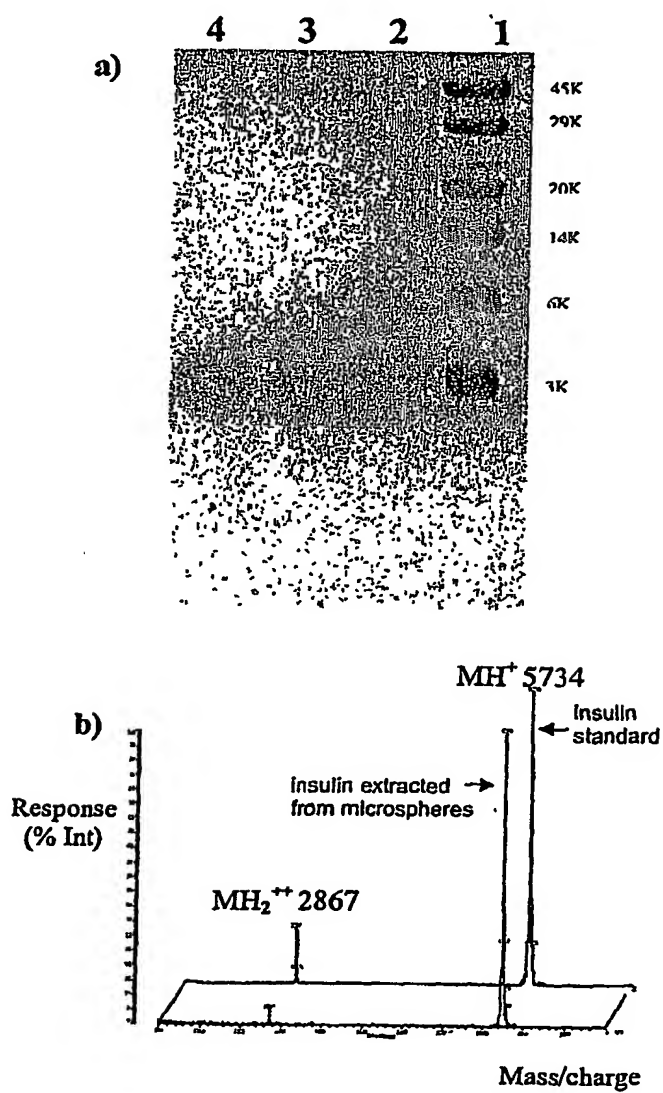
2/8

Figure 2. HPLC chromatogram of insulin sample isolated from composite microspheres by ACN extraction and intact insulin standard.



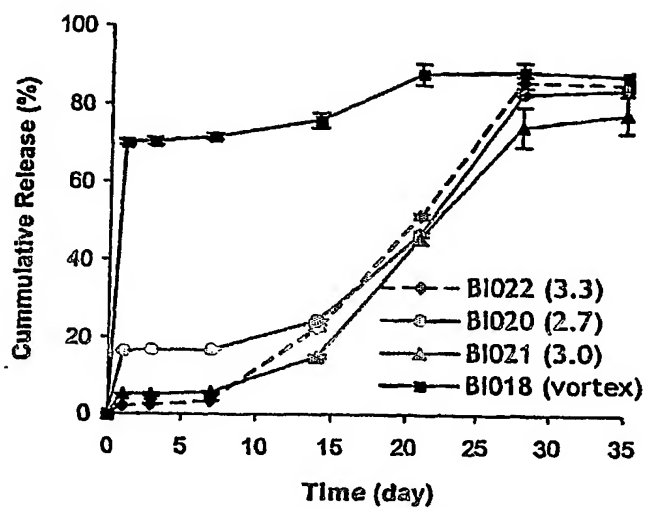
3/8

Figure 3. Characterization of insulin integrity in the composite microspheres (a) SDS-PAGE with DTT. Lane1, Molecular weight marker; Lane 2, Bovine insulin standard; Lane 3, insulin sample from BI021 and lane 4, insulin sample from BI022. (b) MALDI-TOF MS of insulin extracted from composite in comparison to intact standard.



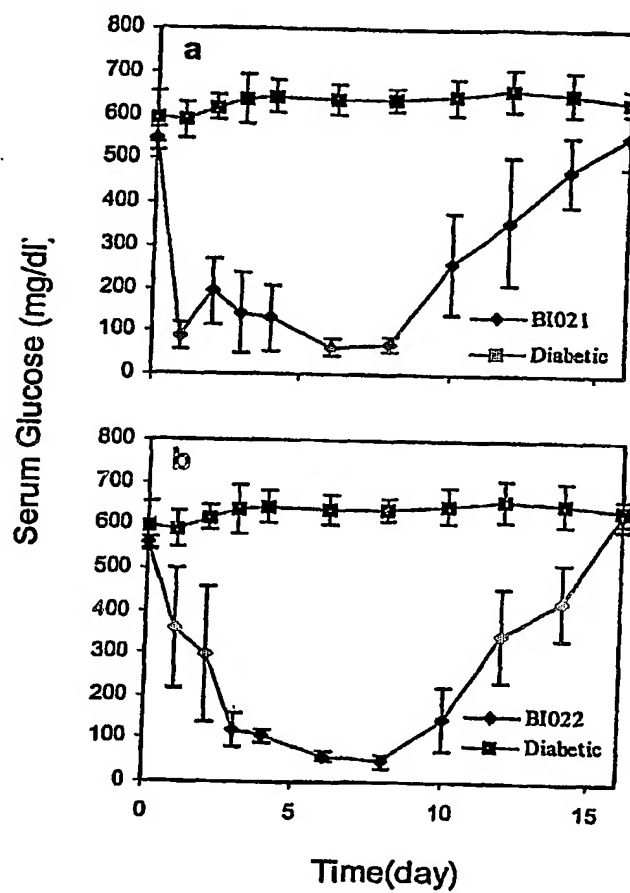
4/8

Figure 4. In vitro release of insulin from composite microspheres in glycine buffer at 37°C. Sonication levels are indicated in ( ).



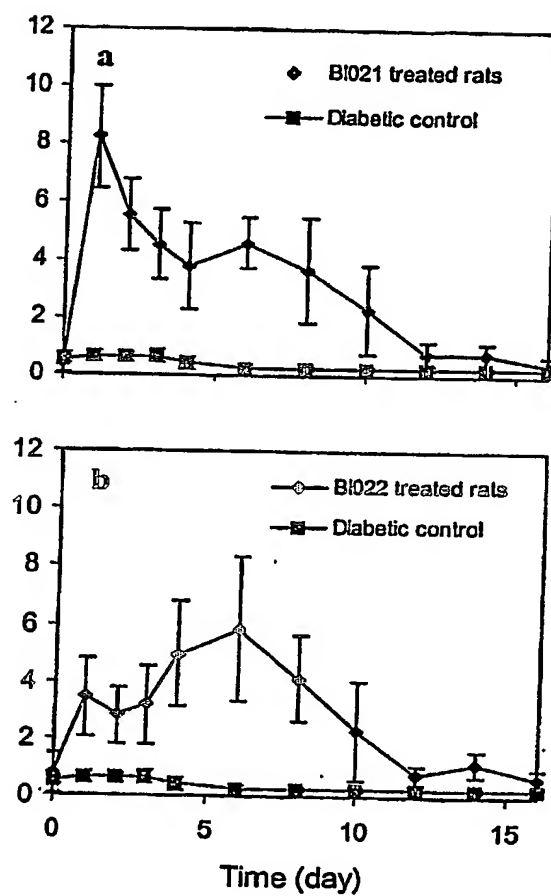
5/8

Figure 5. Serum glucose suppression in diabetic rats treated with insulin loaded composite microsphere batches BI021 (a) and BI022 (b).



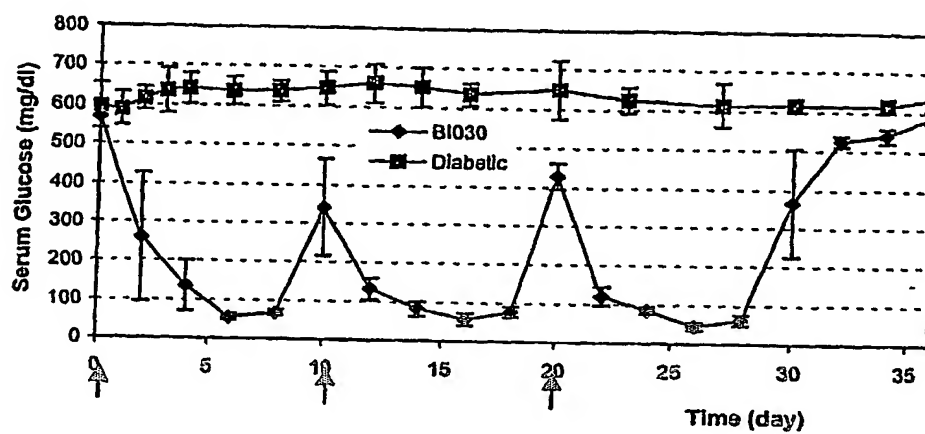
6/8

Figure 6. Serum Insulin level of (a) BI021 and (b) BI022 treated diabetic rats.



7/8

Figure 7. Blood glucose suppression of multiple dosing treatment of insulin loaded composite microspheres (n=8, Dose 80 IU/rat).



8/8

Figure 8. Serum insulin level of multiple dosing treatment of insulin loaded composite microspheres (n=8, Dose 80 IU/rat).

